

### **DETAILED ACTION**

Applicant's amendment in the reply filed on 3/30/2010 is acknowledged. Claim 3 is cancelled. Claims 1, 2, and 4-20 are pending. Claim 6 is withdrawn. **Claims 1, 2, 4, 5, and 7-20 are examined on the merits.**

Any rejection that is not reiterated is hereby withdrawn.

### **Claim Rejections –35 USC § 112, 2<sup>nd</sup>**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4, 5, and 7-20 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recites "Material containing Gnetum extract comprising a solid-liquid mixture of Gnetum gnemon seed material and an aqueous extract of Gnetum gnemon seeds containing stilbenoid with antimicrobial and antioxidatve activity, wherein the seeds are extracted with 15-80% polar organic solvent" (lines1-5). The recitation is very confusing as it is not clear whether the "an aqueous extract of Gnetum gnemon seeds containing stilbenoid" is part of the solid-liquid mixture of Gnetum gnemon seed material, or in addition of the solid-liquid mixture of Gnetum gnemon seed material.

Claim 4 recites "Gnetum liquors comprising a solid removed from the material containing Gnetum extract according to claim 2, wherein the polar organic solvent ethanol". The

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recitation is very confusing, as it is not clear whether the Gnetum liquor comprising the solid or not. The correct recitation should be "A Gnetum liquid according to claim 2, wherein the polar organic solvent is ethanol, and wherein the solid is being removed".

Claim 5 recites "The Gnetum extract according to claim 1, wherein aqueous 50% ethanol solution of the Gnetum extract has an absorption spectrum that indicates the absorption maximum around 320 nm and also, has a thin-layer chromatogram that indicates a spot around Rf value of 0.5". The recitation is very confusing, as it is not clear whether the Gnetum extract has been extracted again with 50% ethanol or not, and it is totally redundant to recites both "aqueous" and "solution" in one sentence. The correct recitation should be "The Gnetum extract according to claim 1, wherein 50% ethanol extract of Gnetum has a maximum absorption around 320 nm and a Rf value of 0.5 in a thin-layer chromatogram". Claims 10 and 13 are rejected for the same reason.

Claim 9 recites "Cosmetics comprising Gnetum extract according to claim 1 as medicinal properties". The recitation is very confusing, as it is not clear how an extract could be properties. Applicant is suggested to recite "A cosmetic comprising the Gnetum extract according to claim 1, wherein the Gnetum extract is the active ingredient of the cosmetic".

Claims 1, 10, and 13 recite "Gnetum extract" (line 1); Claim 2 recites "Material" (line 1); Claim 4 recites "Gnetum liquors" (line 4); Claims 7, 13, and 14 recite "Vegetable extract" (line 1); Claims 8, 12, and 15 recite "Seasoning products" (line 1); Claim 9 recites "Cosmetics" (line 1). The recitations are very confusing. First of all, Applicant is only entitled to one composition, not more than one. Secondly, to be grammatically correct, it is required to include an article

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before a noun. Therefore, the correct recitation should be "A Gentum extract", "A material", "A Gnetum liquor", "A vegetable extract", "A seasoning product", and "A cosmetic".

Claim 7 recites "Vegetable extract comprising Gnetum according to claim 5 being added and mixed to vegetable extract". The recitation is very confusing, as Gnetum itself is a vegetable, and it is not clear whether the 50% ethanol extract of Gnetum is the vegetable extract or the 50% ethanol extract of Gnetum has to be added and mixed with another vegetable extract. Claims 11 and 13 are rejected for the same reason.

Therefore, the metes and bounds of claims are rendered vague and indefinite. The lack of clarity renders the claims very confusing and ambiguous since the resulting claims do not clearly set forth the metes and bounds of the patent protection desired.

All other cited claims depend directly or indirectly from rejected claims and are, therefore, also, rejected under U.S.C. 112, second paragraph for the reasons set forth above.

### **Claim Rejections –35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 2, 4, 5, and 7-20 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Boralle et al (Oligostibenoids from Gnetum venosum, Phytochemistry, 34 (5): 1403-1407,

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1993), in view of Berry (Cyclopropene fatty acids in *Gnetum gnemon* (L.) seeds and leaves, *Journal of the Science of Food and Agriculture*, (1980) Vol. 31, No. 7, pp. 657-662), and further in view of Iliya et al (Iliya et al, Stilbene derivatives from two species of Gnetaceae, *Chem. Pharm. Bull.* 50 (6) 796-801 (2002)), and Qi (Qi, Optimum for extraction processing of stilbene glucoside from *Polygonum multiflorum*, *Zhongcaoyao* (2002), 33(7), 609-611).

This rejection is maintained for reasons of record set forth in the Office Action mailed out on 12/30/2009, repeated below. Applicants' arguments filed have been fully considered but they are not deemed to be persuasive.

Boralle et al teach extracting the seeds of *Gnetum venosum* by exhaustive percolation with EtOH (thus a solid-liquid mixture, an organic solvent, a polar organic solvent). The solution was evaporated (thus solid content is removed) and the residue partitioned between  $\text{CHCl}_3$ , and MeOH. The solvents were evaporated. The residue of the  $\text{CHCl}_3$  solution was fractionated first by CC and finally by TLC. All compounds were purified by HPLC (see title; page 1407, 1st column, 5th paragraph). Boralle et al also teach *Gnetum venosum* contains, besides the stilbenes resveratrol and reponitigentin, oxidative stilbene oligomers such as the dimer gnetic C and the trimers gnetic E, gnetic J and gnetic K (see Abstract).

Boralle et al do not explicitly teach using 15-80% EtOH or 50% EtOH to extract *Gnetum gnemon* seeds, nor do Boralle et al teach mixing *Gnetum* extract to vegetable extract, or an aged *Gnetum* extract or more than 12 h.

Iliya et al teach the family of Gnetaceae is known to contain stilbenoids. The leaves and the fruits are used as food in many parts of tropics. Five new stilbenoids isolated from two species of Gnetaceae. Gnetonoids A and B were obtained from the root of *Gnetum gnemon*.

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Gnemonol C, gnemonoside E and gnetal were isolated from both species (page 796, 1<sup>st</sup> column, 1<sup>st</sup> paragraph).

Berry teaches seed kernels of *Gnetum gnemon*, eaten after boiling or roasting the nuts (see Abstract). Berry teaches that nuts are starchy, astringent and rather bitter in taste that persists even after cooking. The kernels are eaten after removing the shell from the roasted or boiled nuts. They are mashed, moulded into cakes, biscuits or pounded flat into ‘keropok’ (crisps) which are dried in the sun (thus an aged *Gnetum* extract for more than 12 hours) and deep-fried in oil prior to consumption (page 44, 1<sup>st</sup> paragraph). Berry also teaches the young leaves of the plant are consumed as vegetable (page 44, 2<sup>nd</sup> paragraph).

Qi teaches stilbene glucoside was extracted from *Polygonum multiflorum* with 6.0-fold 50% ethanol by refluxing for 30 min. The effect of extraction on stilbene glucoside level was studied by HPLC. The level of stilbene glucoside in the extract was 2-3 times lower than that before extraction. The content of stilbene glucoside in the extract was affected by extractant concentration and extraction time, preferably extractant concentration (see Abstract, the rejection is based on the Abstract, full translation is attached).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to use ethanol (thus polar solvent) to extract stilbene from the seeds or seeds containing material from *Gnetum gnemon* since Boralle et al teach that it is from the seeds of the same genus *Gnetum*, stilbene was isolated. Further more, Iliya et al teach the family of Gnetaceae is known to contain stilbenoids, and stilbene was isolated from the root of claimed species *Gnetum gnemon*. Therefore, an artisan of ordinary skill at the time of the invention would have had a reasonably expected that the seeds or seed containing material of *Gnetum*

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gnemon has the sought properties, which are stilbenes, namely gnetin C, gnemonocide A and Gnemonocide D, and it is deemed that the claimed material stilbenes would necessarily have the claim designated antimicrobial and/or antioxidative function.

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to boil the Gnetum gnemon kernels (the same as seeds) and leaves (thus mixing with vegetable extract) together (thus a polar extract water) and then to consume since Berry teaches both the kernel and leaves can be eaten.

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to use 50% ethanol to extract stilbenoid since Qi teaches using 50% ethanol to extract stilbene glycoside (thus a stilbenoid) and the content of stilbene glucoside in the extract was affected by extractant concentration.

Since all of the references teach using plant materials from genus Gnetum, one of ordinary skill in the art would have been motivated to make the modifications and combine the references together.

Since the references teach extracting the claimed material Gnetum seeds with the claimed solvent ethanol, it is deemed that the extracts would intrinsically have the claimed absorption spectrum and Rf value.

The intended use of the composition was analyzed for patentable weight. It is deemed that the preamble 'breathes life' into the claims in that the prior art product must not be precluded for use as cosmetic or seasoning products. It is deemed that the composition disclosed by the cited reference is not precluded for carrying out the intended function of the claims.

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From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Applicant argues that “Qi et al disclosed the *extraction of stilbene glucoside* from *P. multiflorum* with 50% EtOH is best under heat reflux for 30 min. The peak of resveratrol (aglycon: production by hydrolysis of stilbene glucoside), however, is not recognized on HPLC. This result shows that glucosidase does not act at all and this extraction depends only on the penetration of solvent and the solubility of the stilbene glucoside which is most soluble in 50% EtOH. A glucosidase is inactivated under the heat reflux in solvent, because Qi et al. does not consider the presence and the action of the glucosidase in *P. multiflorum*.

*The constituents in the extracts of other Polyogonum* extracts are for example:

1) Kiem PV et al., *Arch. Pharm. Res.*, 2008, 31(11), 1477-82.

They disclose extracting a whole plant of *P. hydropiper* with MeOH to isolate phenylpropanoid esters of sucrose.

2) L.O. Demirezer et al., *Pharmaceutical Biology*, 2006, 44(6), 462-66.

They disclose extracting aerial parts of *P. alpinum* with MeOH to isolate flavonol glycosides.

3) Xiao-Bai Sun et al., *Chemistry of Natural compounds*, 2007, 43(5), 563-65.

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They disclose extracting whole roots of *P.bistorta* to isolate triterpenoids, cumarin and steroid.

4) F. Yang et al., *J. Chromatography A*, 2001, 919(2), 443-8.

They disclose separating resveratrol and anthraglycosides from the crude extract of *P. cuspidatum* by high-speed counter-current chromatography.

The above examples demonstrate that each plant possesses different constituents, even if the plants belong to the same *Polygonanceae* genus” (pages 5-6).

Applicant argues that “The yields of constituents in Iliya et al. by extraction of root and stem with acetone and MeOH are very poor. This result shows *merely extraction and isolation of stilbenoids*. They do not also notice the presence and the action of glucosidase in the root and stem. Wallance et al. extract leaves of *G. gnemon* with acetone and water (1:1) to isolate C-glycosyl flavones distinct from the stilbenoids (*Phytochemistry*, 1978, 17, 1809-1810)” (page 6).

Applicant argues that “In Boralle et al. *G. venosum* kernels are extracted by exhaustive percolation with EtOH to isolate stilbenoids containing gnetin C except their glucosides (gnemonoside A etc.). They disclose merely carrying out the extraction of the kernels and *isolation of the stilbenoids*, and do not notice the presence and action of glucosidase in the kernels, as well” (page 6, last paragraph bridging page 7).

This is not found persuasive. Qi teaches extracting stilbene with 50% ethanol, thus one of the ordinary skills in the art would have been motivated to extract stilbene with 50% ethanol. It is



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not relevant what action of glucosidase is, as glucosidase is not in the claims. Also it is noted that extraction temperature is not recited in the claims.

Applicant argues that “Berry discloses extracting cyclopropene fatty acids from *G. gnemon* seeds and merely introducing the seeds and leaves as foodstuffs, but does not suggest existence of stilbenoids and application of the extract to seasonings, antibacterial substances and cosmetics” (page 7, 2nd paragraph).

This is not found persuasive. First of all, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Secondly, the intended use of the composition was analyzed for patentable weight. It is deemed that the preamble ‘breathes life’ into the claims in that the prior art product must not be precluded for use as a cosmetic, seasoning, or antibacterial composition. It is deemed that the composition disclosed by the cited reference is not precluded for carrying out the intended function of the claims.

Applicant argues that “The cited art alone merely discloses the extraction and isolation of stilbenoids generally. The claimed invention, however, differs from the combination of the cited art in utilization of the aging which converts the stilbene glucoside into the aglycon by hydrolysis without addition of some glucosidases. The aging means action (for example, hydrolysis) of glucosidase in endosperms. The applicants found out the phenomenon given only gnemonoside A by extraction of Emping Belinjo produced by heat-processing of endosperms

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(Comparison I). The enzyme reaction (hydrolysis) is affected the concentration of polar organic solvent, soak (extract) temperature and time. On the other hand, skilled artisans who do not notice this phenomenon make the enzyme reaction inhibited and inactivated by use of single polar organic solvent and heat reflux” (page 7, 3<sup>rd</sup> paragraph). Applicant also argues that “The applicants investigated extraction and aging of endosperms under various conditions to discover *the aqueous extractant containing the polar organic solvent concentration in the range of 15% to 80%* and soak temperature below about 70°C. The extractant ranging in the concentration from 40% to 60% resulted in gnetin C as major composition in contrast to gnemonoside A. Thus the composition ratio of gnetin C in the extract has been controlled. The extract containing antimicrobial gnetin C brings about extension of the shelf life of foods and cosmetics in addition to improvement of flavor of vegetable extract” (page 7, last paragraph from the bottom).

Applicant further argues that “In the case of polar organic solvent concentration below 10%, gnemonoside A in matrix of endosperms is hydrolyzed by glucosidase to form slightly soluble gnemonoside D and insoluble gnetin C, which separate in the vicinity of the glucosidase to inhibit dissolution of gnemonoside A. The hydrolysis is consequently depressed” (page 7, last paragraph bridging page 8). Applicant at last argues that “In the case of polar organic solvent concentration in the range of 15% to 80%, hydrolysis of gnemonoside A gives gnemonoside D which is continuously hydrolyzed to gnetin C, since all of gnemonoside A, gnemonoside D and gnetin C dissolve in the solvent. In the case of polar organic solvent concentration over 90%, hydrolysis of gnemonoside A, which is insoluble in the solvent, does not proceed. As noted above, an artisan of ordinary skill cannot expect from the cited art that such a glucosidase exists in the endosperms, not to mention making antibacterial and antioxidative gnetin C from

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gnemonoside A through gnemonoside D under appropriate conditions which are the aqueous extractant containing the polar organic solvent concentration in the range of 15% to 80% and soak temperature below about 70°C. The utilization of the glucosidase by aging first led to better yield of such a gnetin C. This result enables to apply foods and cosmetics as seasoning, antibacterial substance and antioxidant” (page 8).

This is not found persuasive. Berry teaches seed kernels of *Gnetum gnemon*, eaten after boiling or roasting the nuts (see Abstract). Berry teaches that nuts are starchy, astringent and rather bitter in taste that persists even after cooking. The kernels are eaten after removing the shell from the roasted or boiled nuts. They are mashed, moulded into cakes, biscuits or pounded flat into ‘keropok’ (crisps) which are dried in the sun (thus an aged *Gnetum* extract for more than 12 hours). Thus the limitation of “aging” is met. 7-37-08: In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., glucosidase, hydrolysis temperature, soak temperature below about 70°C, or the concentration of each claimed components) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant's arguments have been fully considered but they are not persuasive, and therefore the rejections in the record are maintained.

### **Conclusion**

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Qiuwen Mi whose telephone number is 571-272-5984. The examiner can normally be reached on 8 to 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Qiuwen Mi/

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